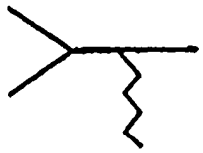
FORMS OF IMMUNE AUGMENTATION

1. FREE ANTIBODY + PEPTIDE

mAb-A (ANTI-CD3) peptide

2. HETEROCONJUGATE (ANTIBODY-PEPTIDE)



3. BIFUNCTIONAL mAb/LIGAND CONJUGATE

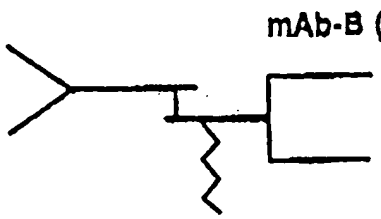


FIGURE 1

FIGURE 2:

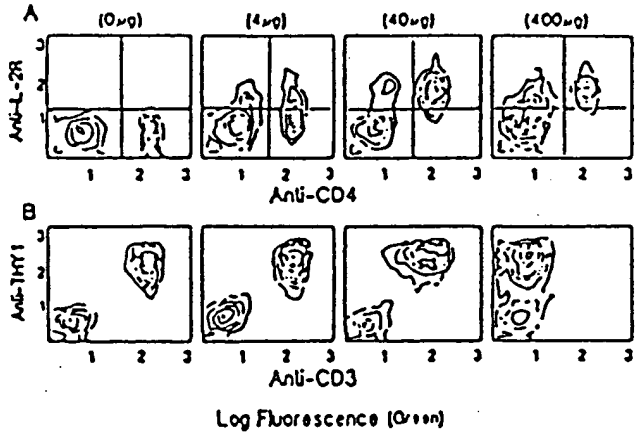

A
(0 μg)
(4 μg)
(40 μg)
(400 μg)
Anti-IL-2R
Anti-CD4
B
Anti-THY1
Anti-CD3
Log Fluorescence (Green)

FIGURE 3:

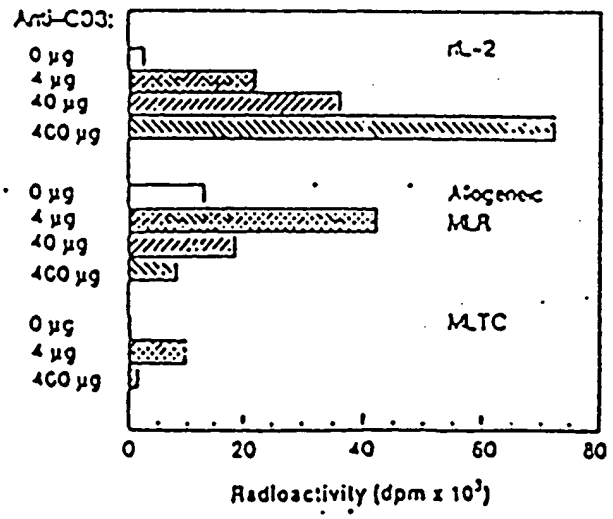

Anti-CD3:
0 µg
4 µg
40 µg
400 µg
IL-2
0 µg
4 µg
40 µg
400 µg
Allogeneic MLR
0 µg
4 µg
400 µg
MLTC
0
20
40
60
80
Radioactivity (dpm x 10³)

FIGURE 4:

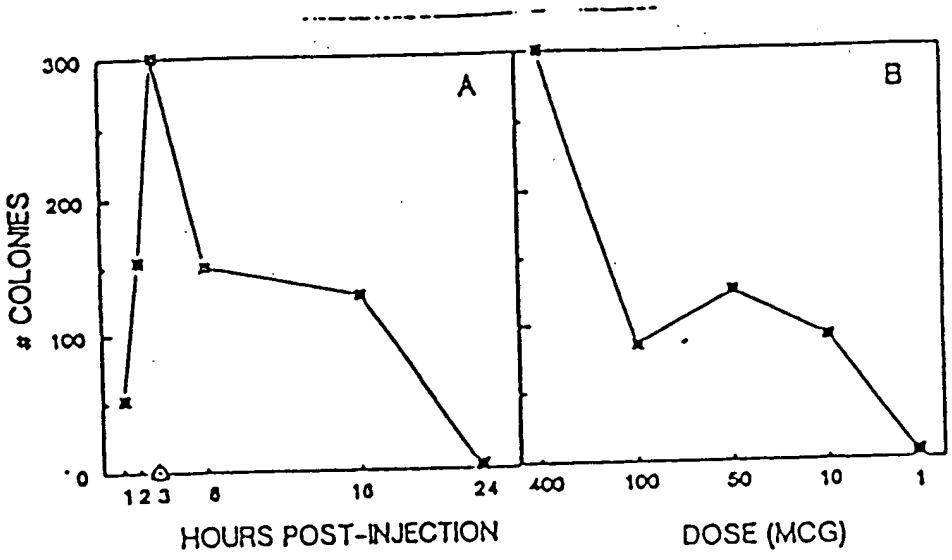
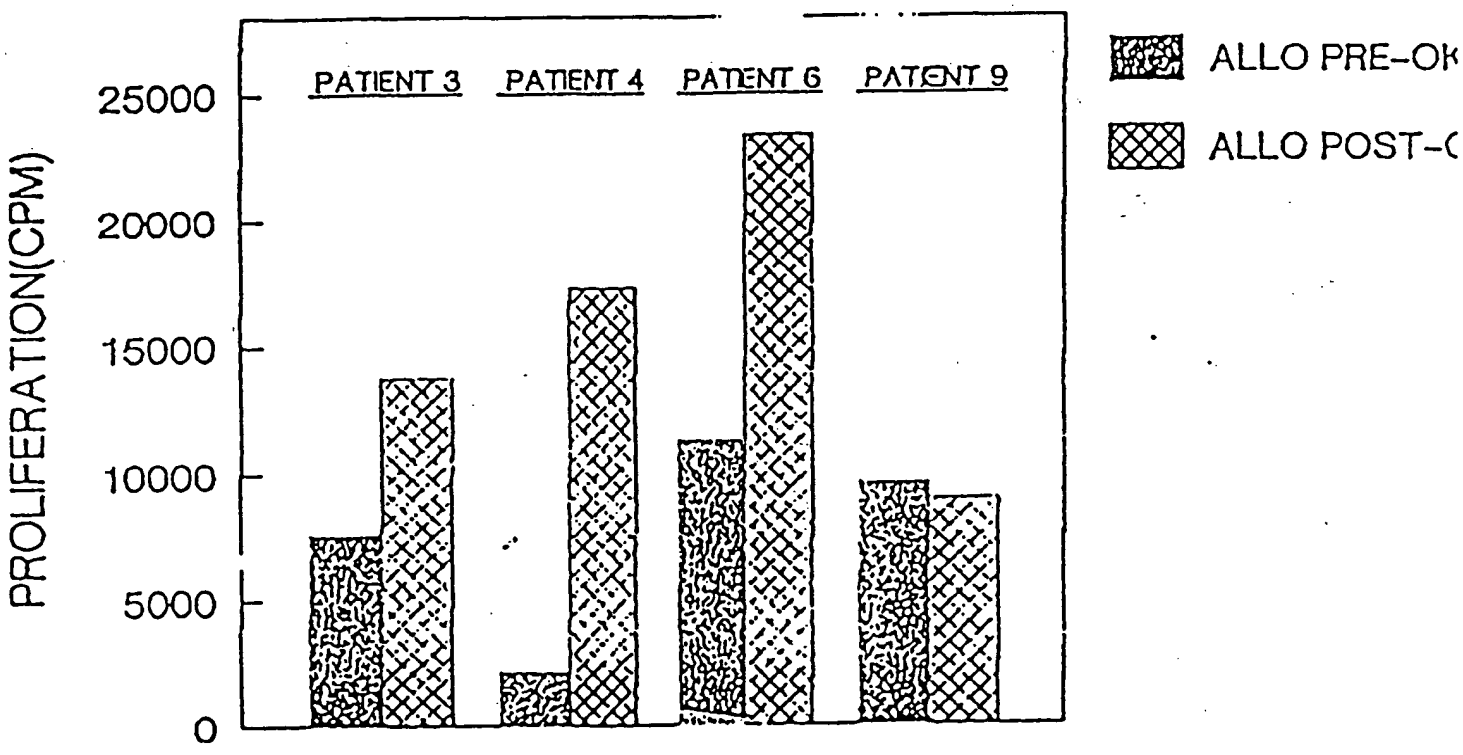

300
200
100
0
COLONIES
A
B
1 2 3
6
10
24
400
100
50
10
1
HOURS POST-INJECTION
DOSE (MCG)

FIGURE 5 A:



(MCG) HOURS POST-INJECTION DOSE

FIGURE 5 B:

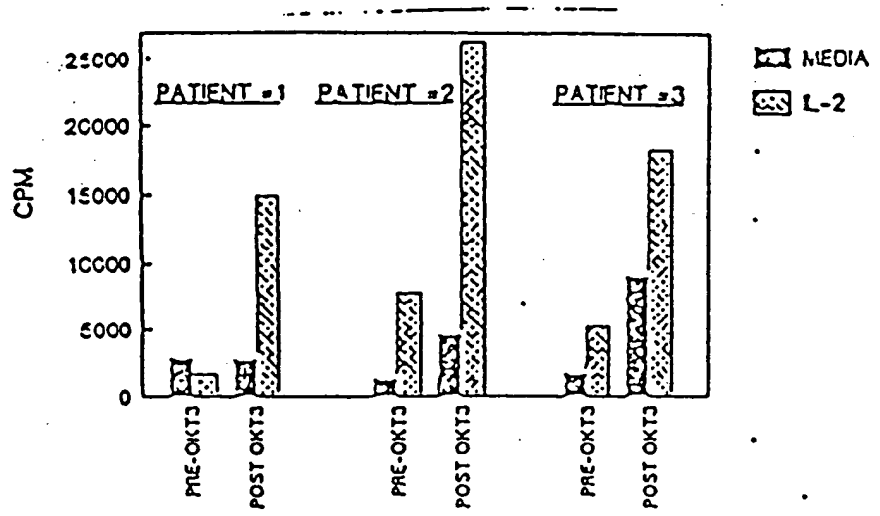

CPM
25000
20000
15000
10000
5000
0
PATIENT #1
PATIENT #2
PATIENT #3
MEDIA
IL-2
PRE-OKT3
POST OKT3
PRE-OKT3
POST OKT3
PRE-OKT3
POST OKT3

FIGURE 6:

ANTI-KLH ANTIBODIES IN MICE TREATED WITH KLH USING PBS, CFA, OR ANTI-CD3 AS IMMUNOADJUVANTS

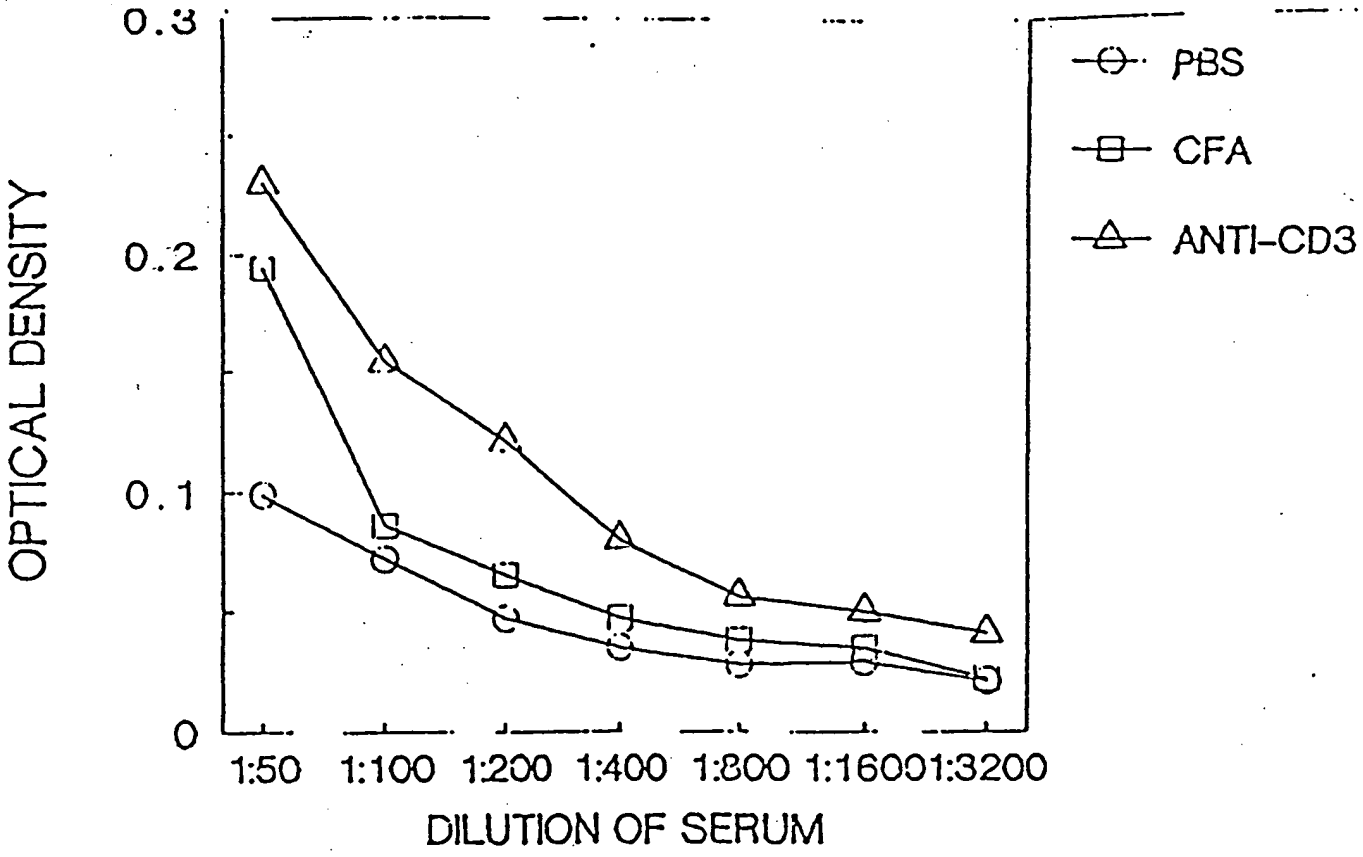
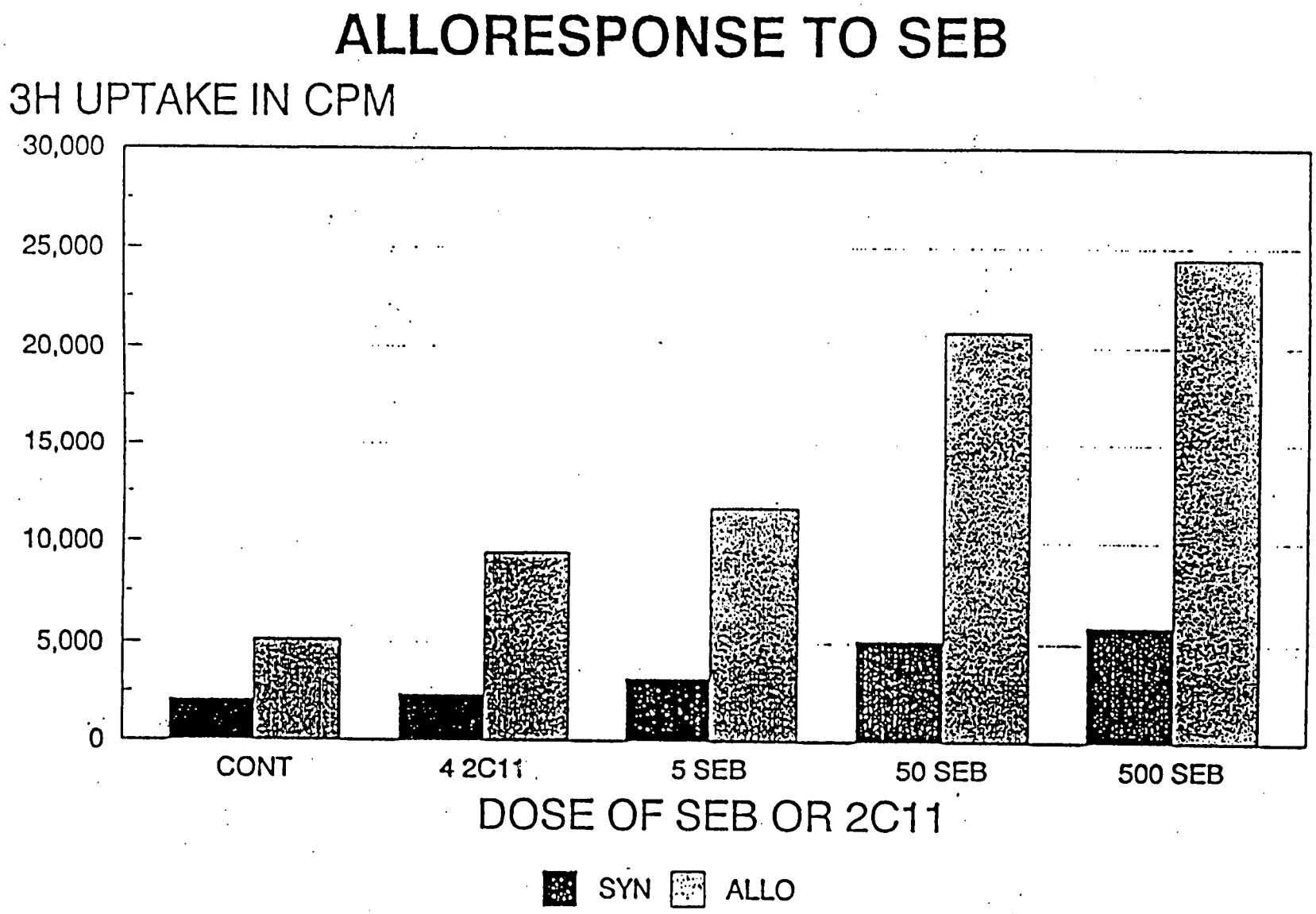


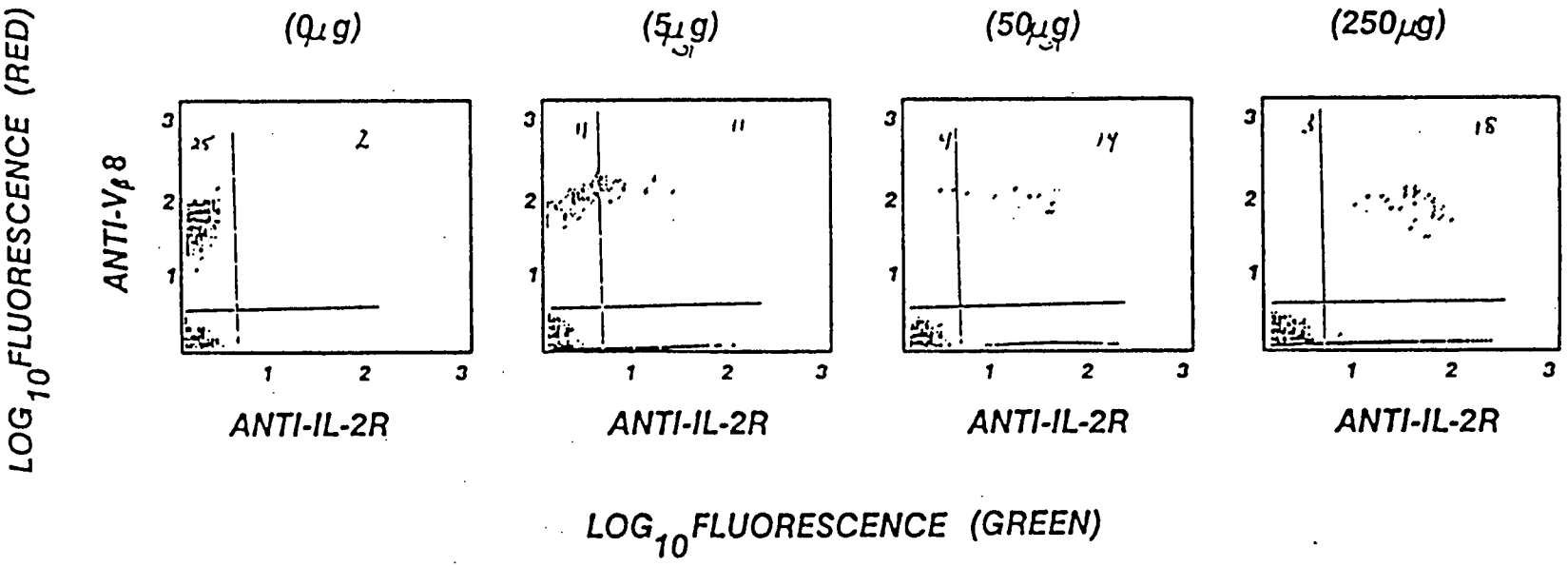
FIGURE 7:



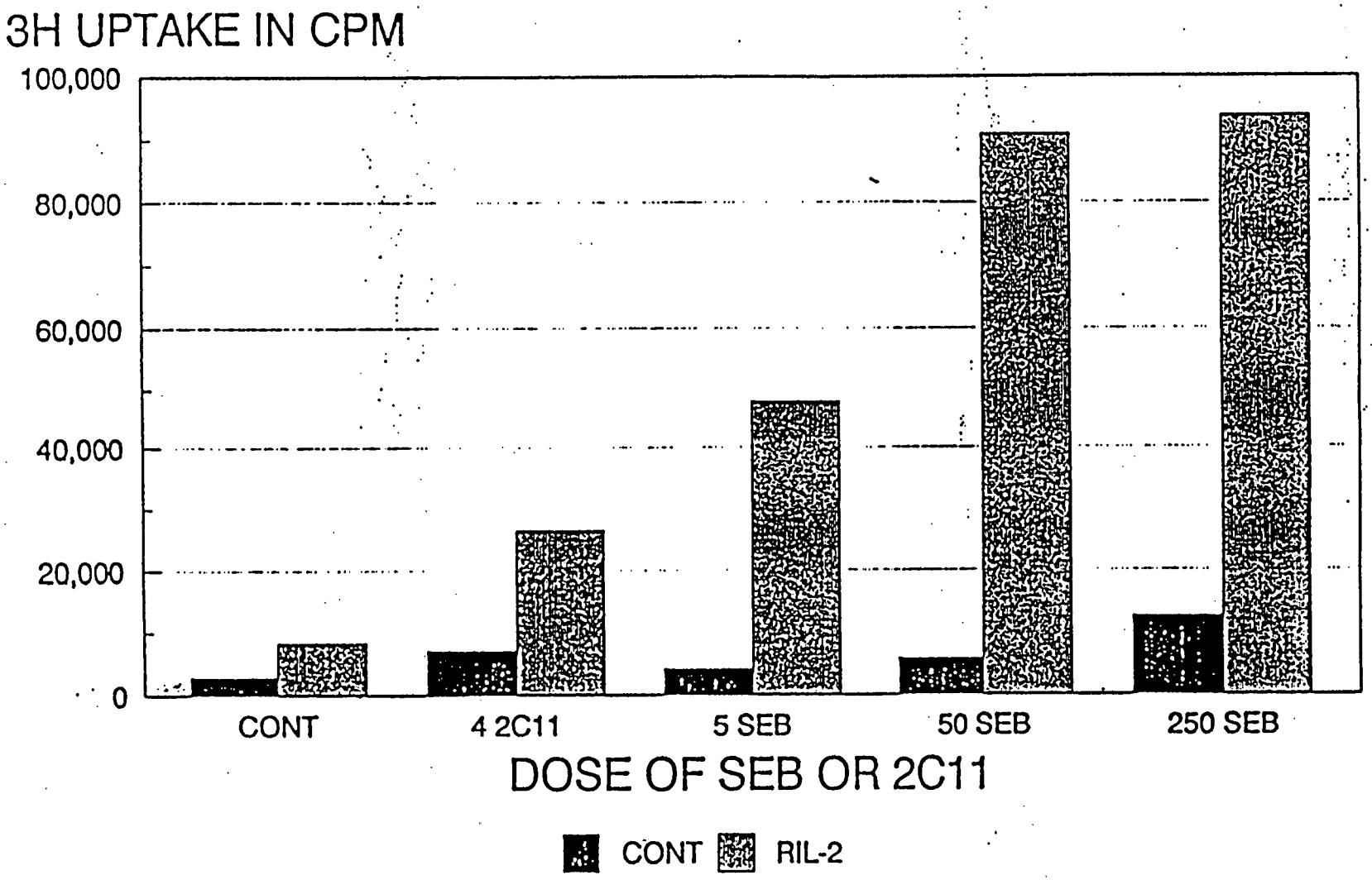
in C3H mice at 18 hr.

FIGURE 8:

IL-2R EXPRESSION ON T CELLS FROM SEB TREATED MICE (18hr.)



PROLIFERATIVE RESPONSE TO SEB



in C3H mice at 18 hr. using lymph node

FIGURE 10:

EXPANSION OF V_β 8+ CELLS IN SEB-TREATED MICE

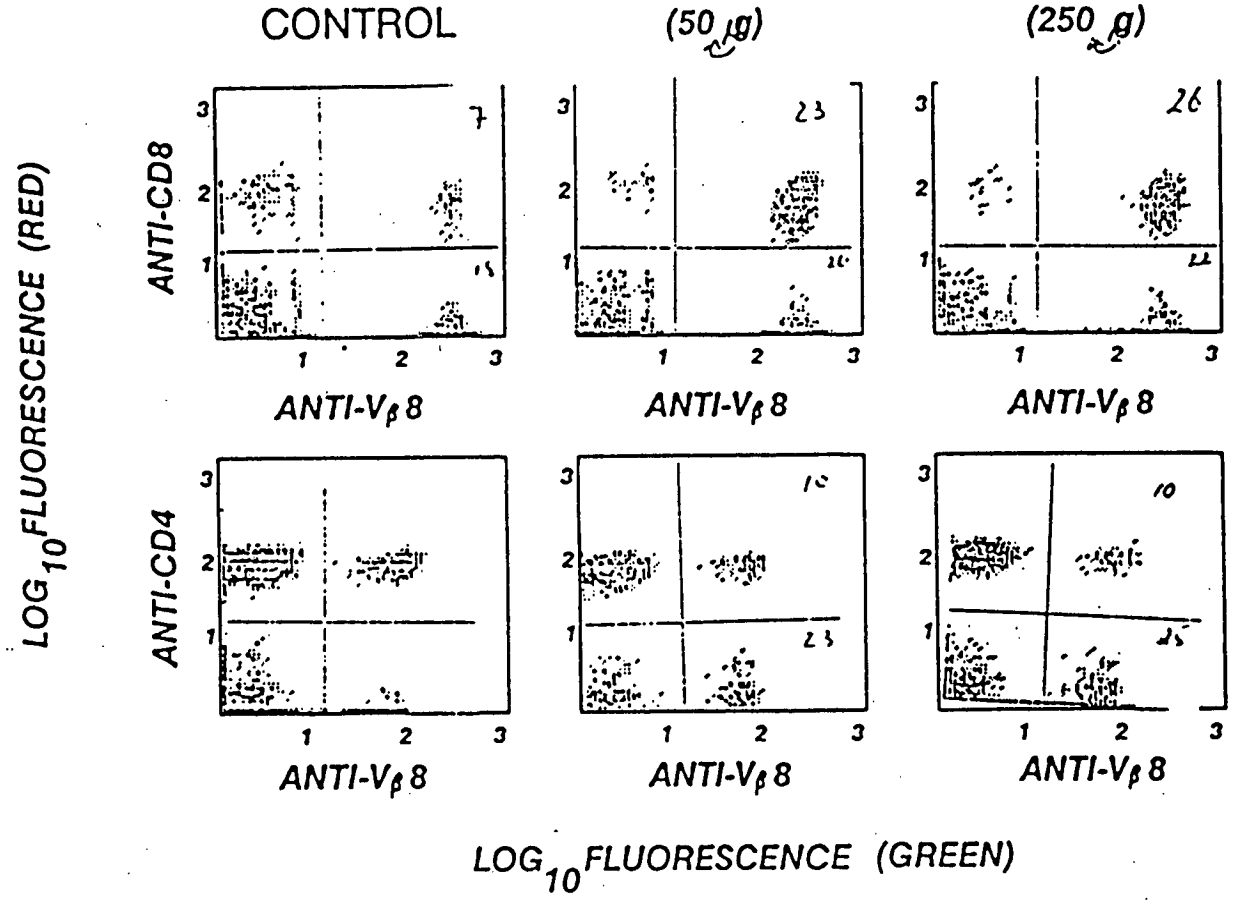


FIGURE 11:

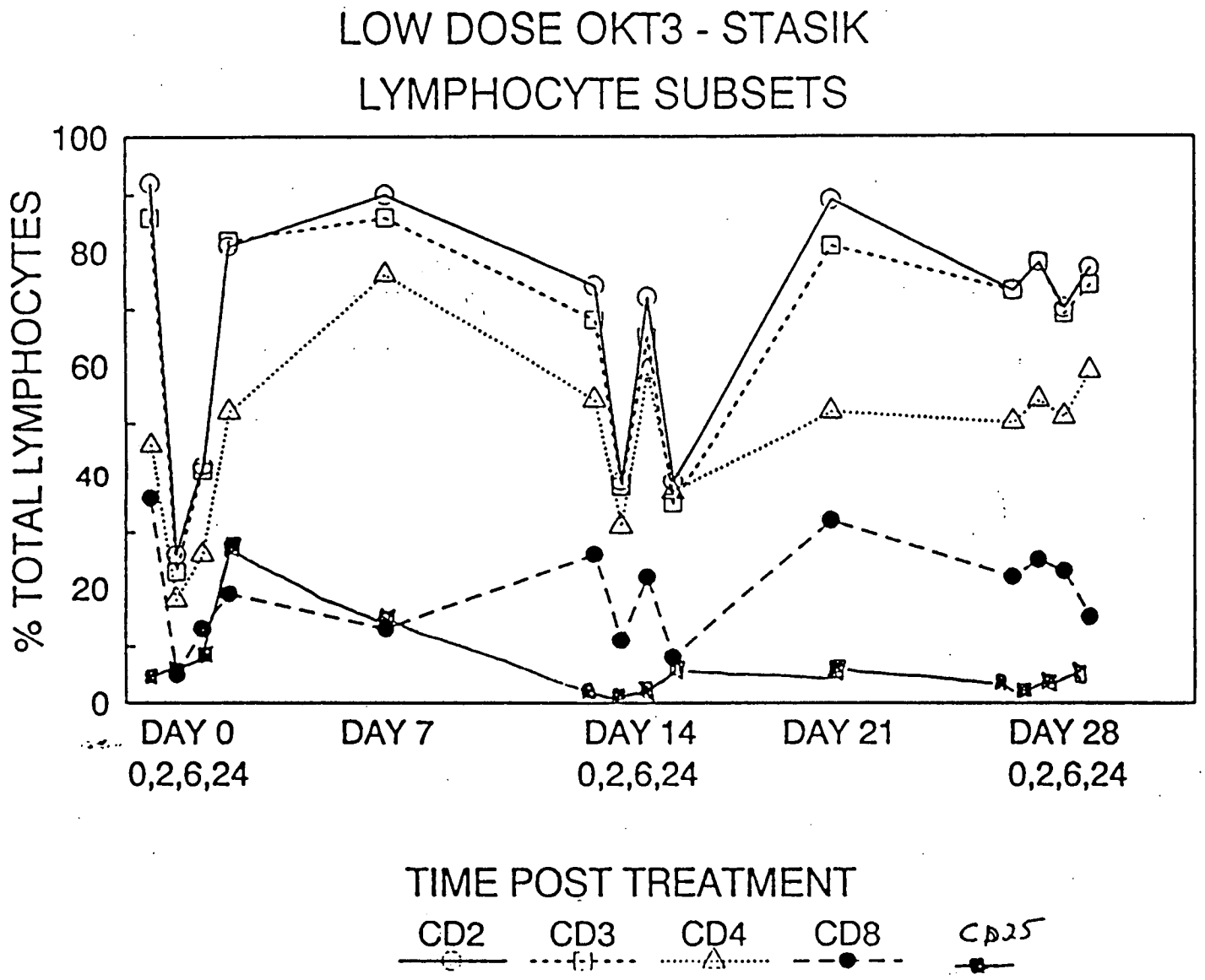
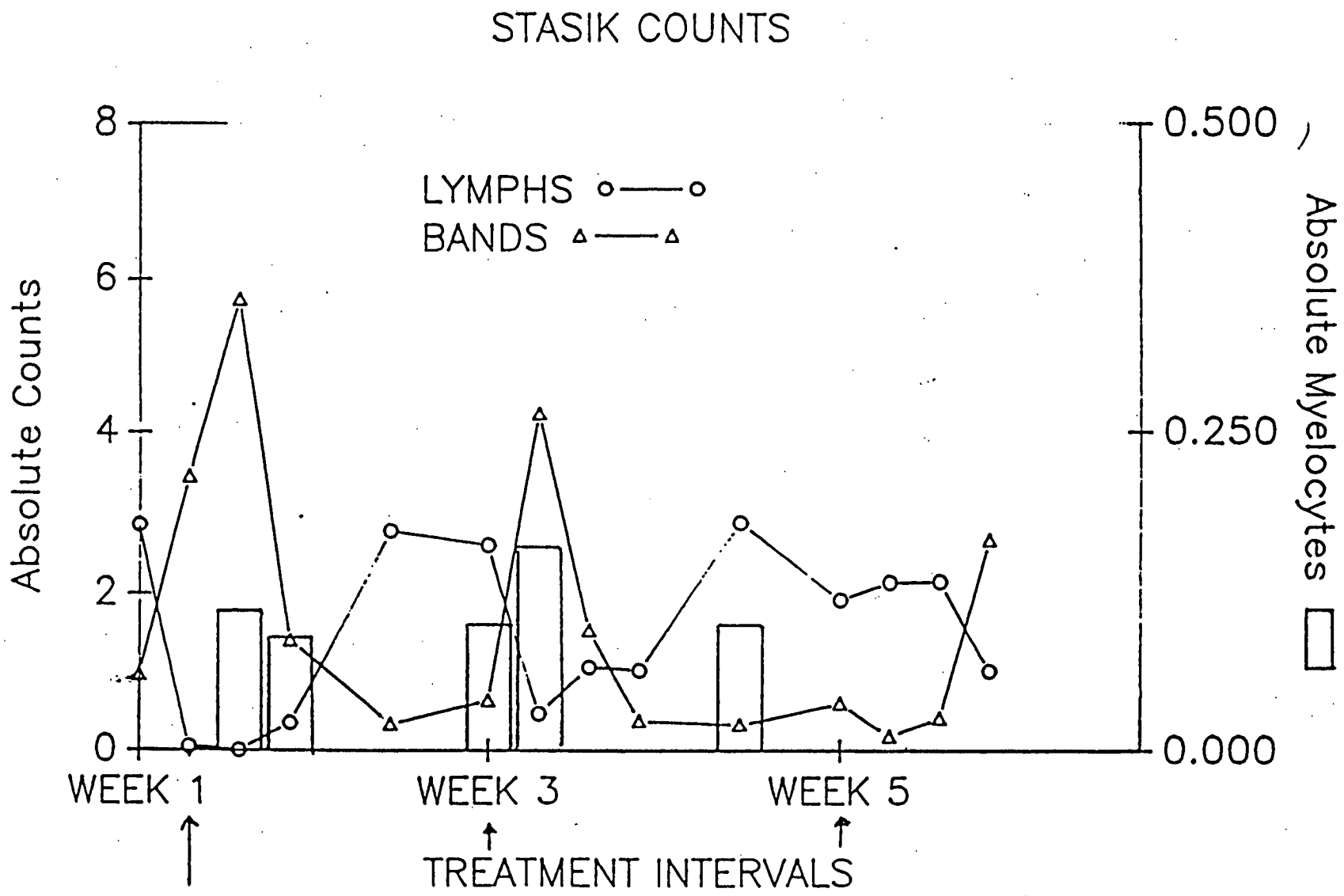

LOW DOSE OKT3 - STASIK
LYMPHOCYTE SUBSETS
% TOTAL LYMPHOCYTES
100
80
60
40
20
0
DAY 0
0,2,6,24
DAY 7
DAY 14
0,2,6,24
DAY 21
DAY 28
0,2,6,24
TIME POST TREATMENT
CD2
CD3
CD4
CD8
CD25

FIGURE 12:


STASIK COUNTS
LYMPHS
BANDS
Absolute Counts
Absolute Myelocytes
8
6
4
2
0
0.500
0.250
0.000
WEEK 1
WEEK 3
WEEK 5
TREATMENT INTERVALS

ANTI-CD3 TREATMENT ABROGATES GVHD
B10.BR --> (B10 x B10.BR)F1 [500R]

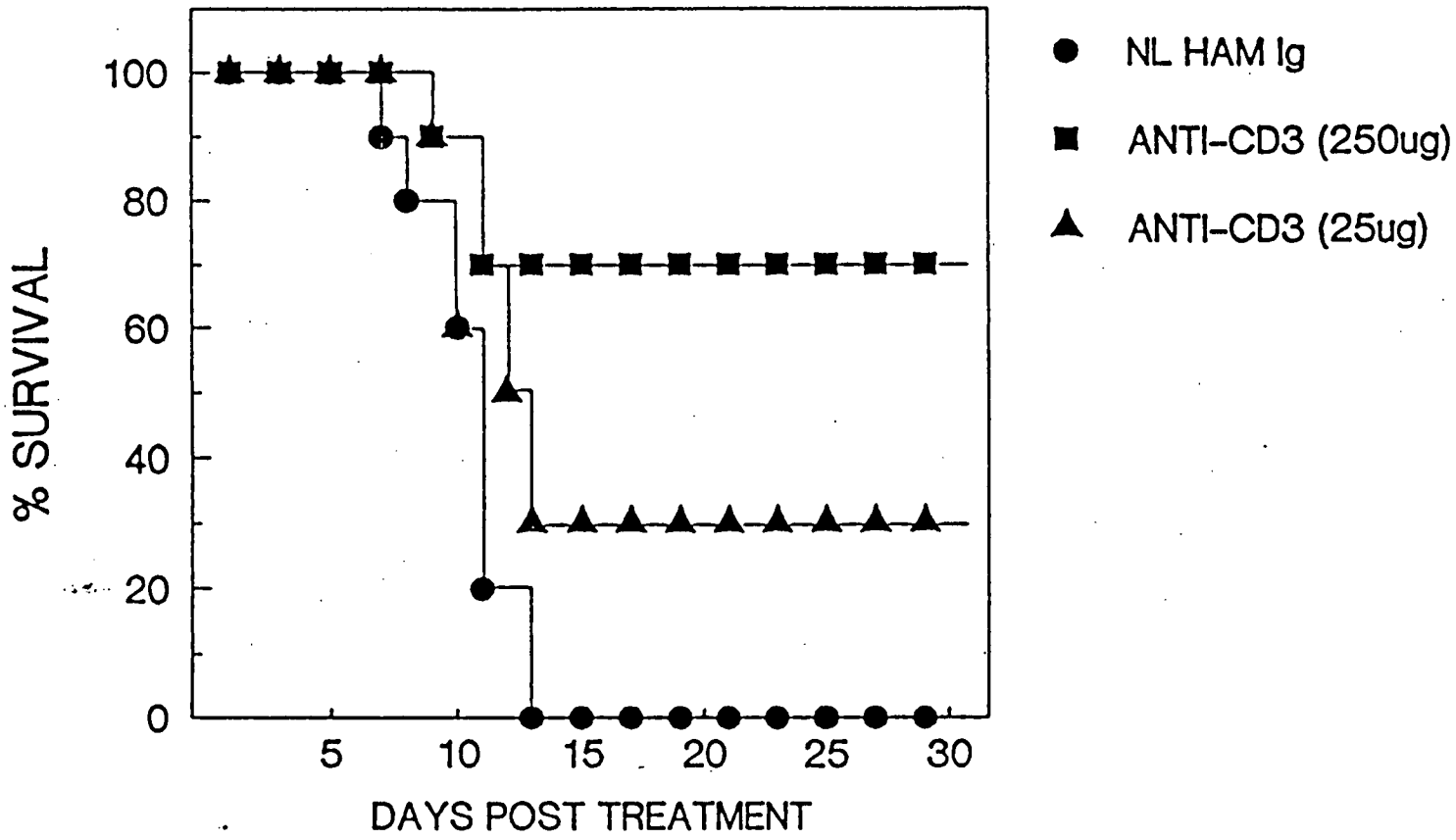


FIGURE 14:

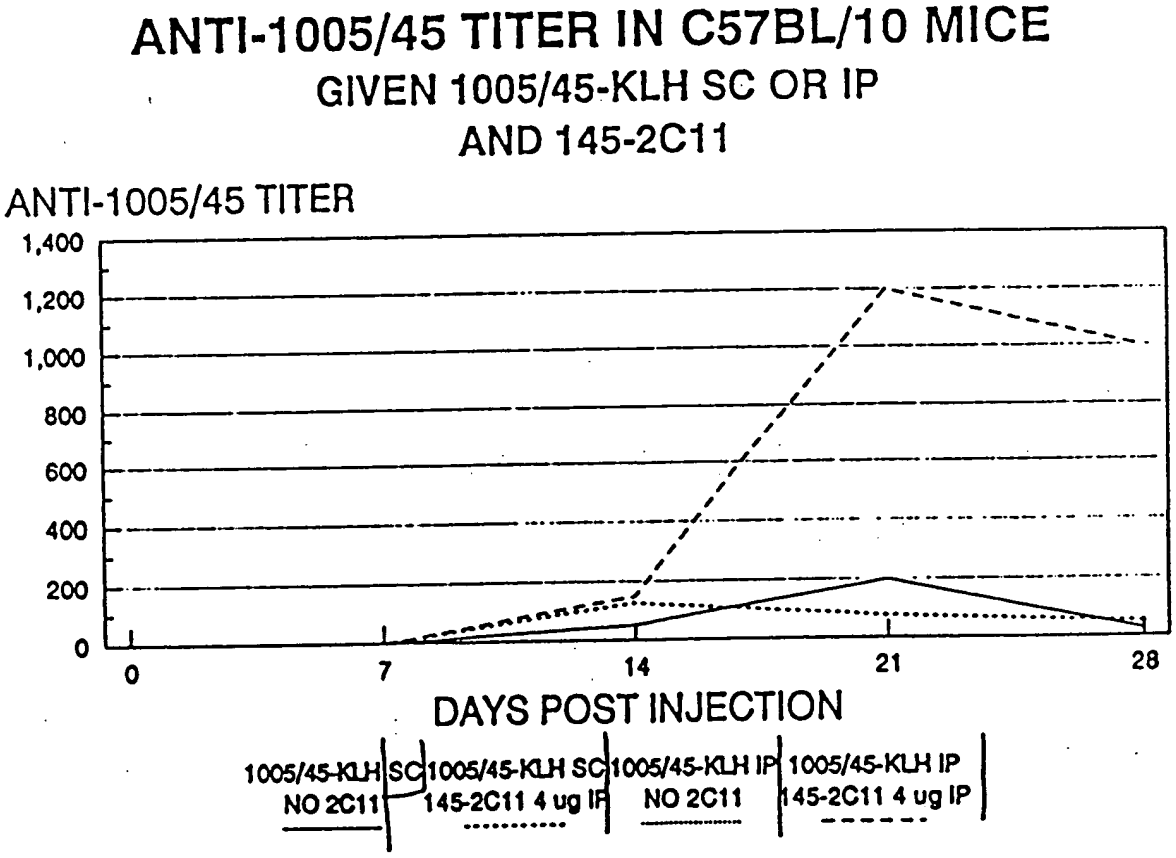

ANTI-1005/45 TITER IN C57BL/10 MICE
GIVEN 1005/45-KLH SC OR IP
AND 145-2C11
ANTI-1005/45 TITER
1,400
1,200
1,000
800
600
400
200
0
0
7
14
21
28
DAYS POST INJECTION
1005/45-KLH SC NO 2C11
1005/45-KLH SC 145-2C11 4 ug IP
1005/45-KLH IP NO 2C11
1005/45-KLH IP 145-2C11 4 ug IP

FIGURE 15:

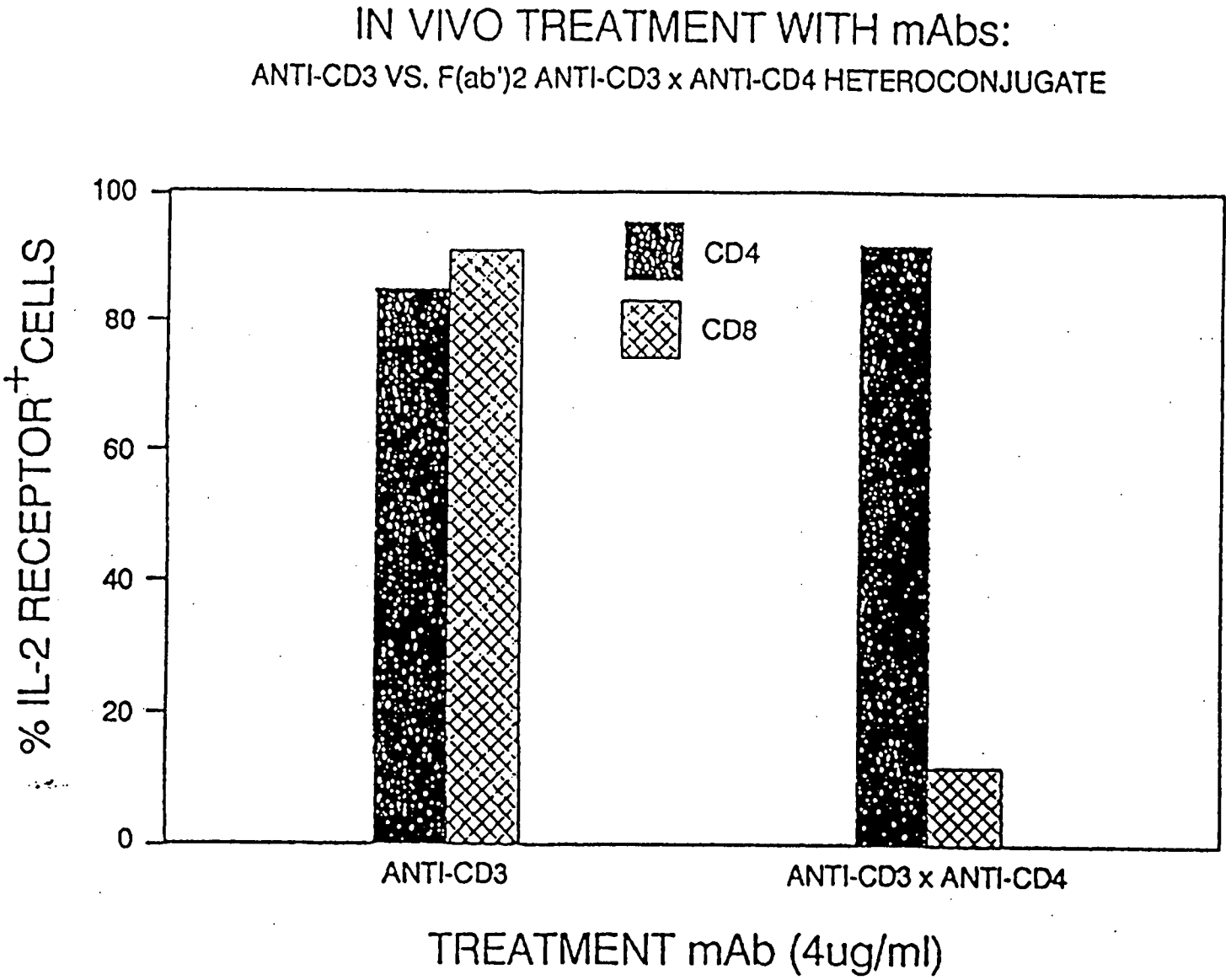

IN VIVO TREATMENT WITH mAbs:
ANTI-CD3 VS. F(ab')2 ANTI-CD3 x ANTI-CD4 HETEROCONJUGATE
% IL-2 RECEPTOR+CELLS
100
80
60
40
20
0
CD4
CD8
ANTI-CD3
ANTI-CD3 x ANTI-CD4
TREATMENT mAb (4ug/ml)

FIGURE 16:

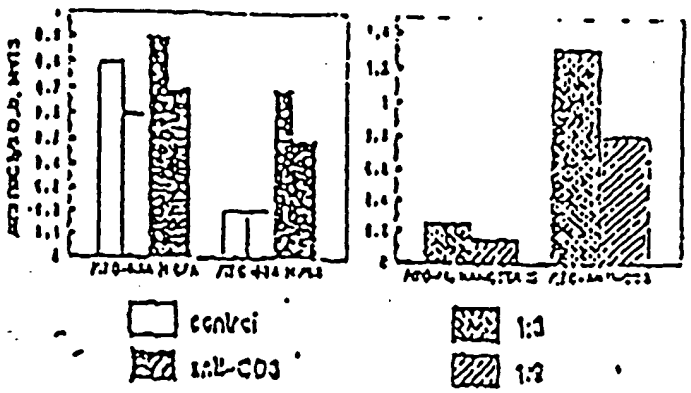
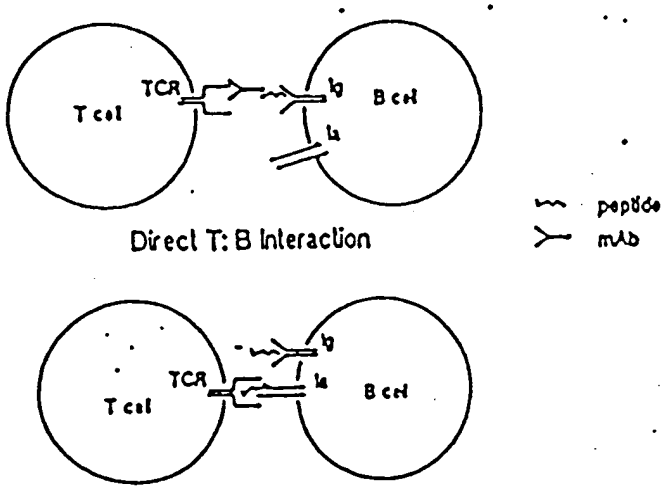
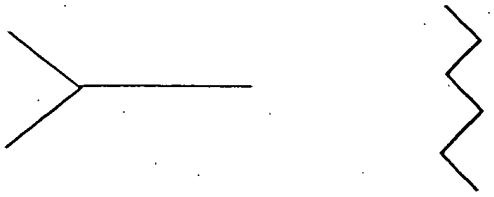


FIGURE 17:

TWO MODELS OF TB COLLABORATION



MHC RESTRICTED Ag RECOGNITION



mAb-A(ANTI-CD3) PEPTIDE

FIG. 1A

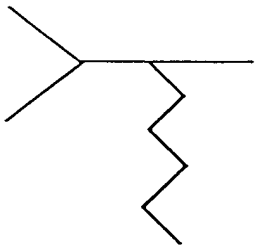


FIG. 1B

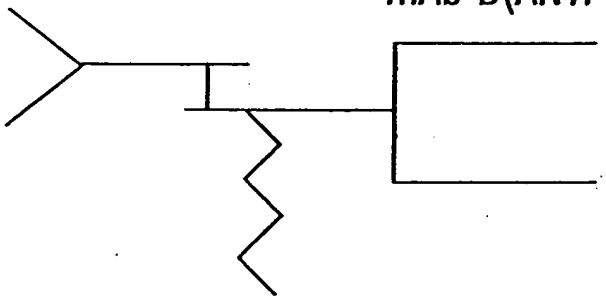


FIG. 1C

FIG. 2A-1

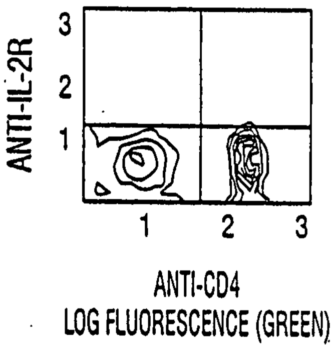


FIG. 2A-2

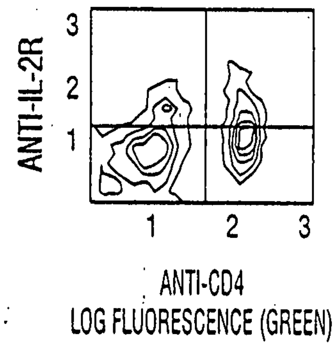


FIG. 2A-3

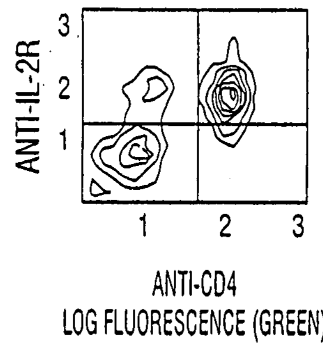


FIG. 2A-4

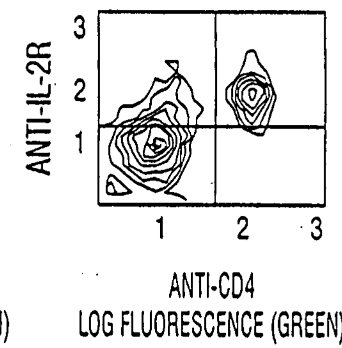


FIG. 2B-1

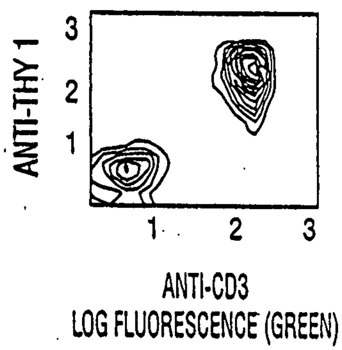


FIG. 2B-2

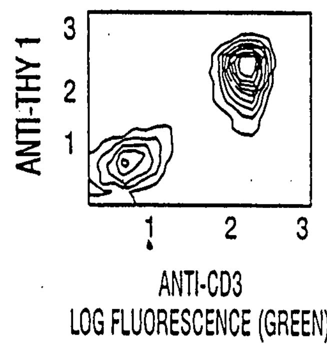


FIG. 2B-3

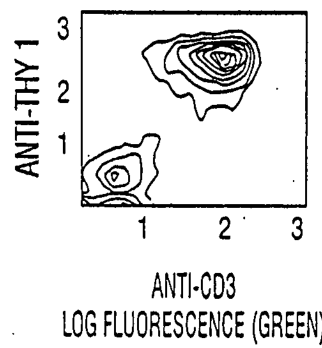
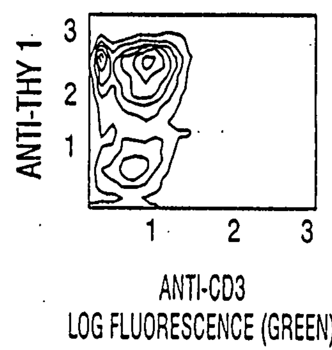


FIG. 2B-4



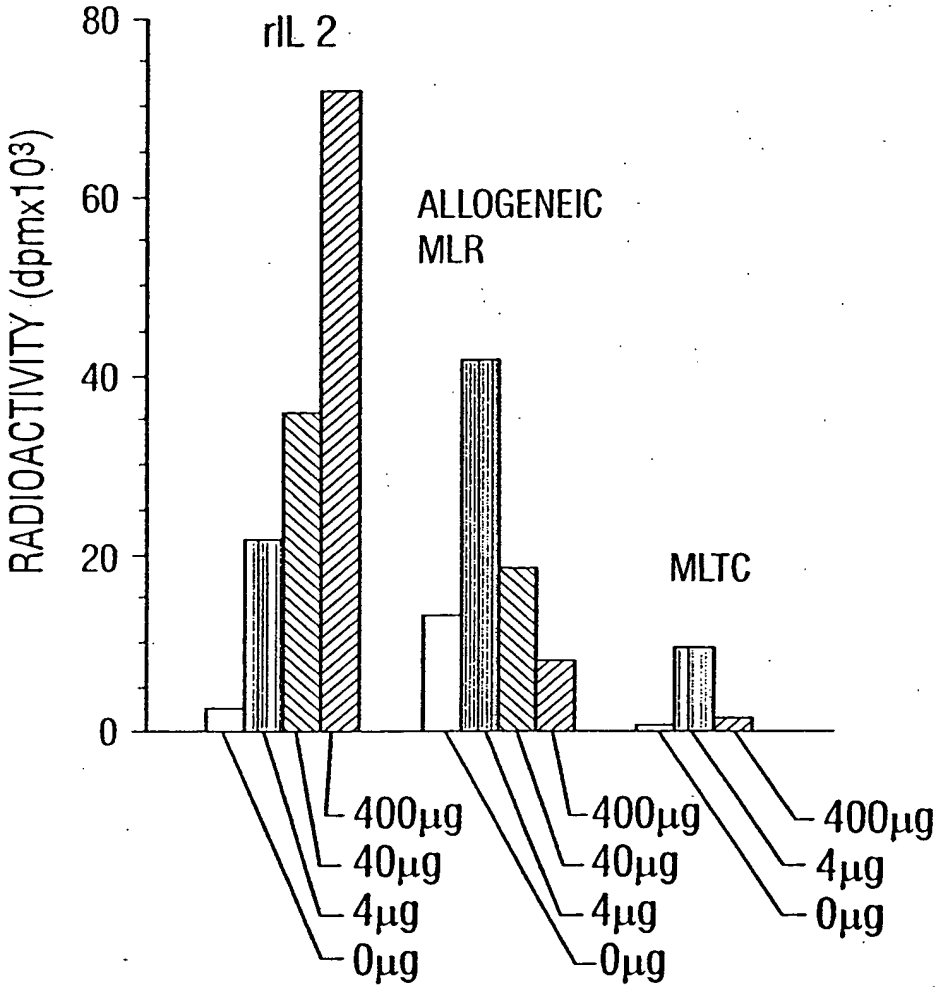

80
60
40
20
0
RADIOACTIVITY (dpmx10³)
rIL 2
ALLOGENEIC
MLR
MLTC
400μg
40μg
4μg
0μg
400μg
40μg
4μg
0μg
400μg
4μg
0μg

FIG. 3

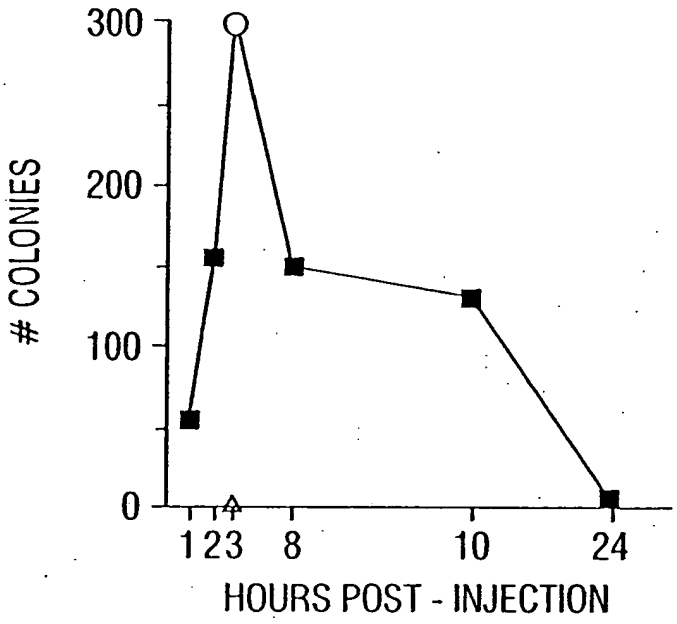

300
200
100
0
COLONIES
1 2 3
8
10
24
HOURS POST - INJECTION

FIG. 4A

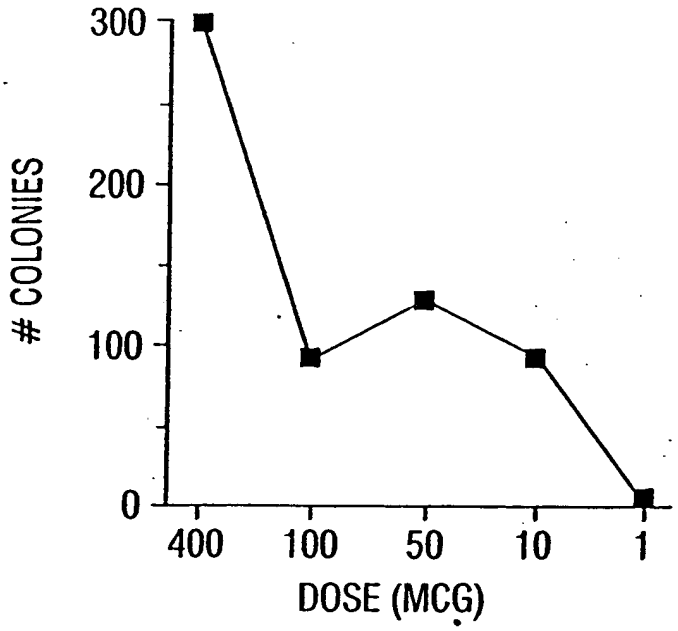

300
200
100
0
COLONIES
400
100
50
10
1
DOSE (MCG)

FIG. 4B

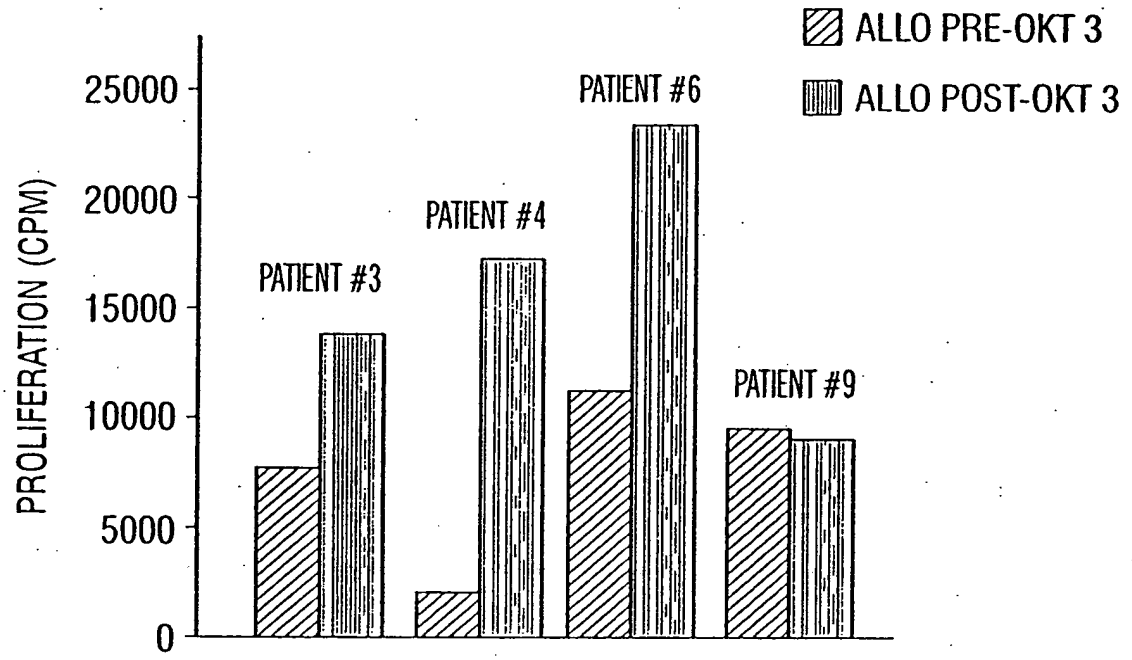

ALLO PRE-OKT 3
ALLO POST-OKT 3
PROLIFERATION (CPM)
25000
20000
15000
10000
5000
0
PATIENT #3
PATIENT #4
PATIENT #6
PATIENT #9

FIG. 5A

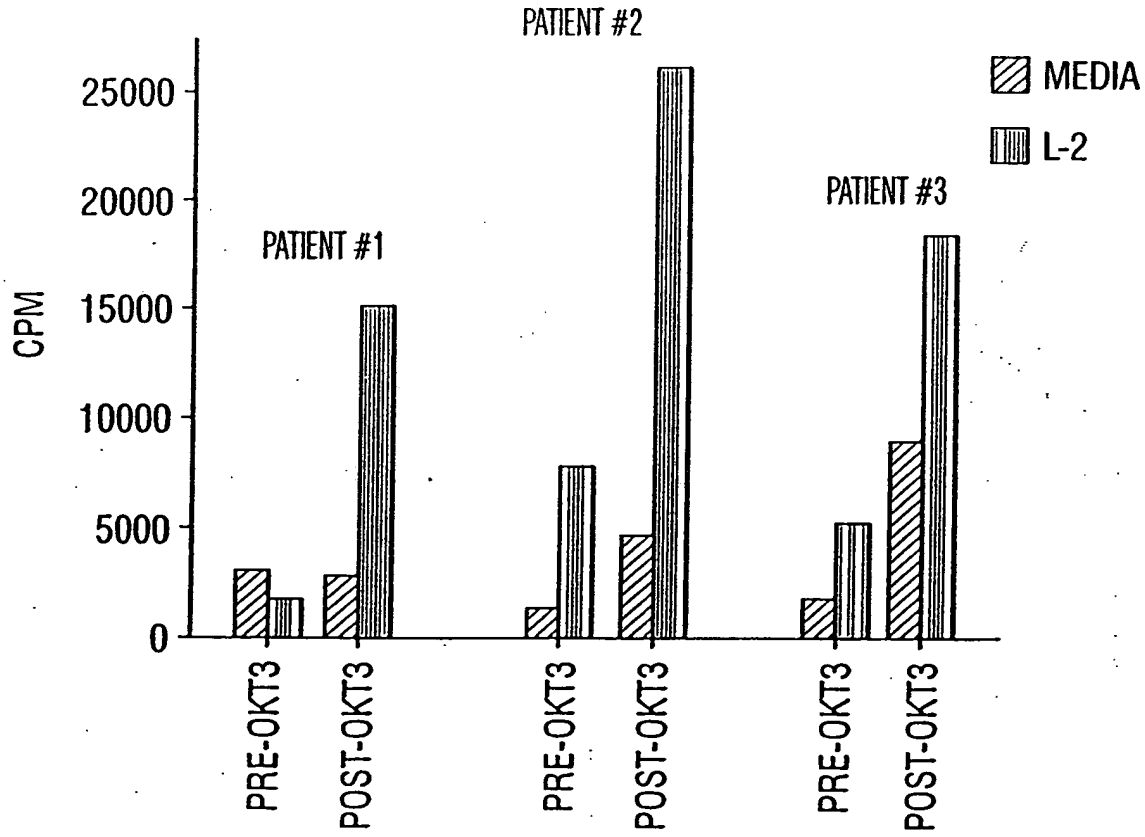

MEDIA
L-2
CPM
25000
20000
15000
10000
5000
0
PATIENT #1
PATIENT #2
PATIENT #3
PRE-OKT3
POST-OKT3
PRE-OKT3
POST-OKT3
PRE-OKT3
POST-OKT3

FIG. 5B

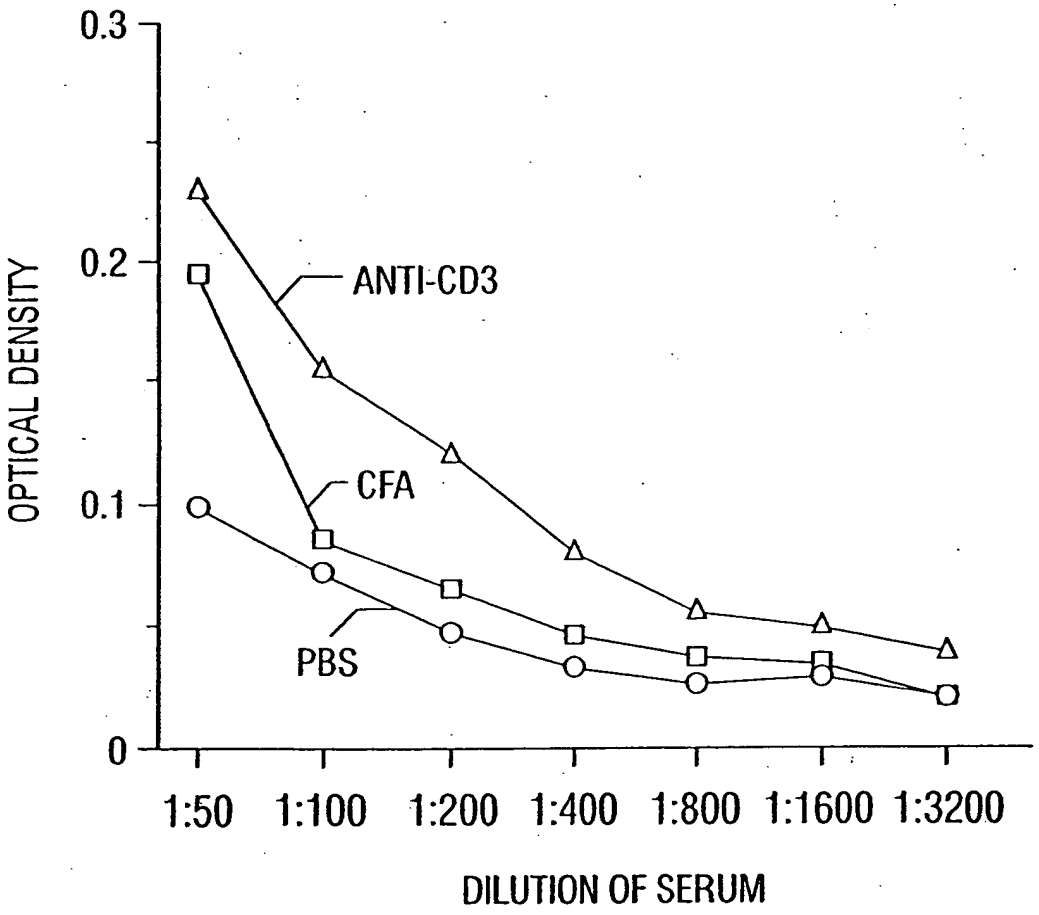

0.3
0.2
0.1
0
OPTICAL DENSITY
ANTI-CD3
CFA
PBS
1:50
1:100
1:200
1:400
1:800
1:1600
1:3200
DILUTION OF SERUM

FIG. 6

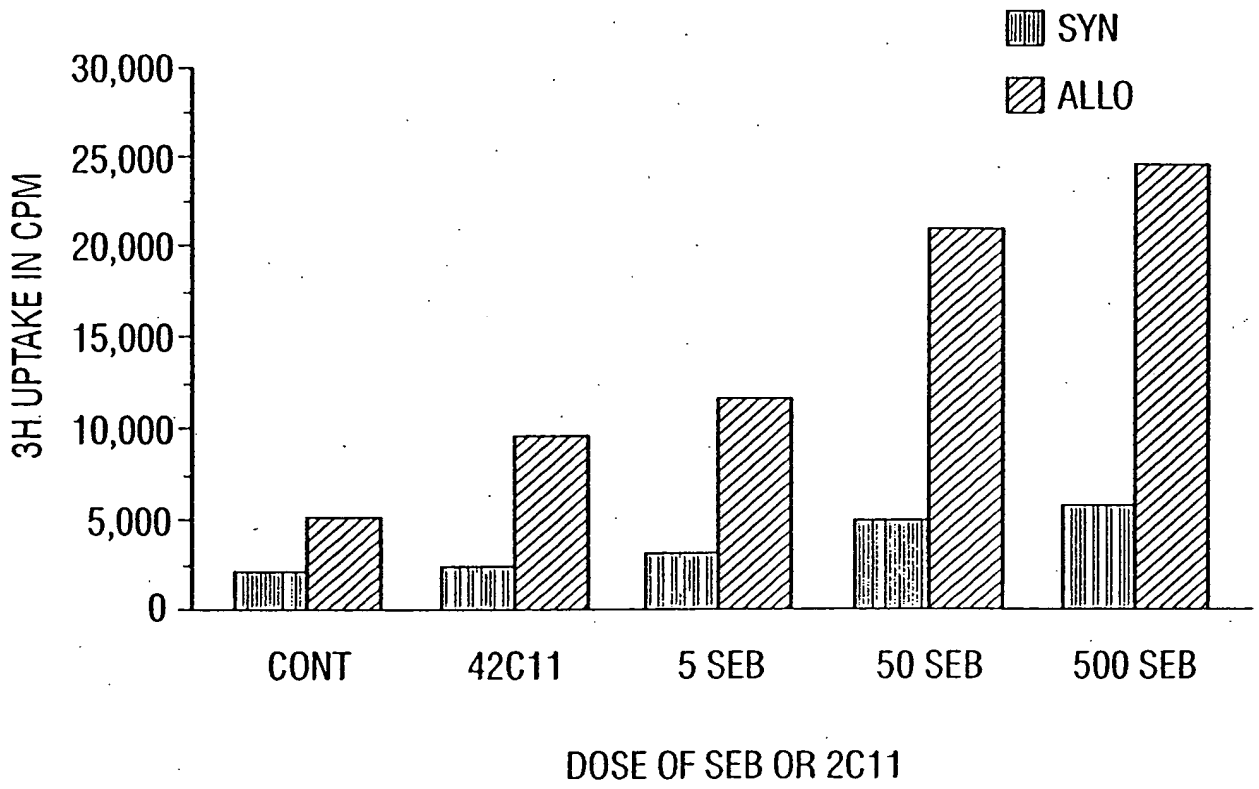

SYN
ALLO
30,000
25,000
20,000
15,000
10,000
5,000
0
3H UPTAKE IN CPM
CONT
42C11
5 SEB
50 SEB
500 SEB
DOSE OF SEB OR 2C11

FIG. 7

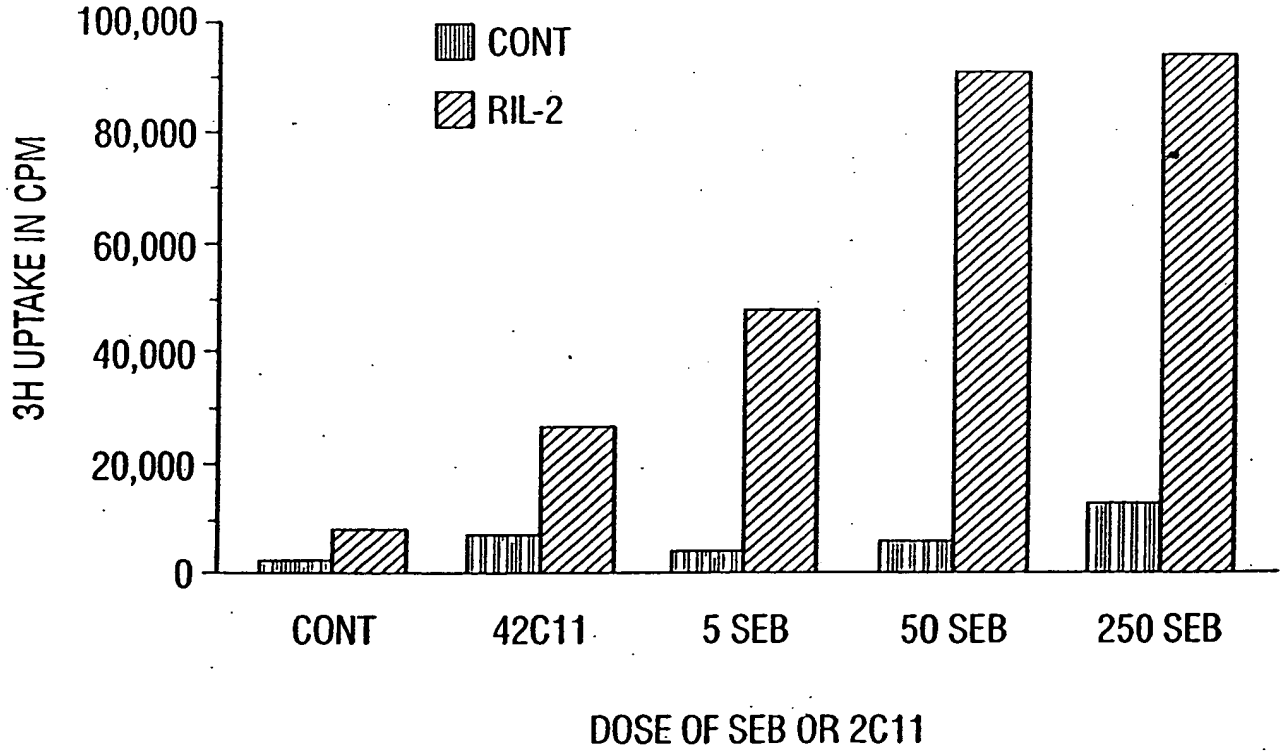

CONT
RIL-2
100,000
80,000
60,000
40,000
20,000
0
3H UPTAKE IN CPM
CONT
42C11
5 SEB
50 SEB
250 SEB
DOSE OF SEB OR 2C11

FIG. 9

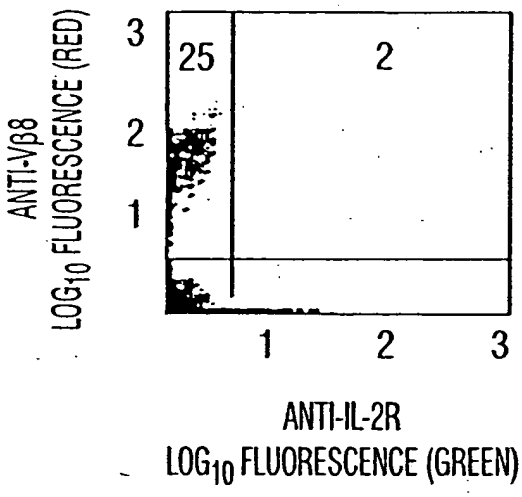


FIG. 8A

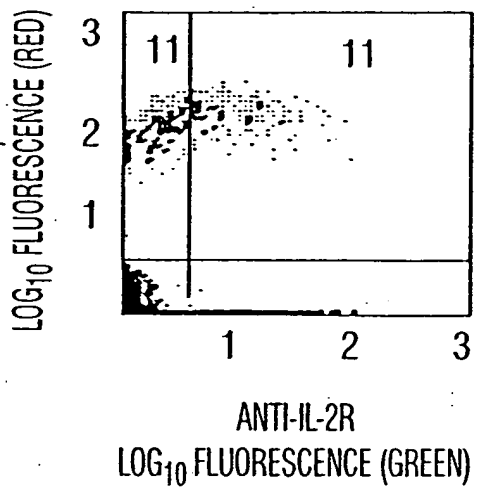


FIG. 8B

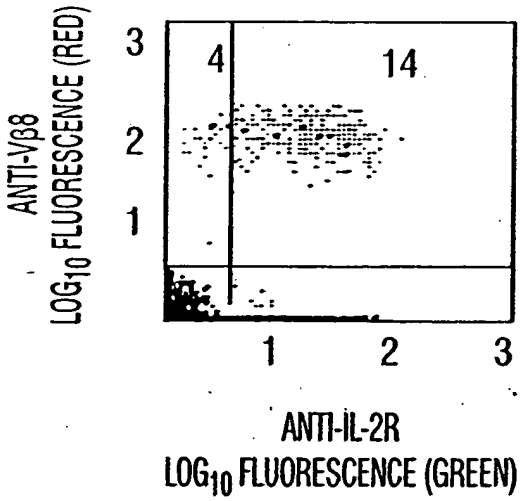


FIG. 8C

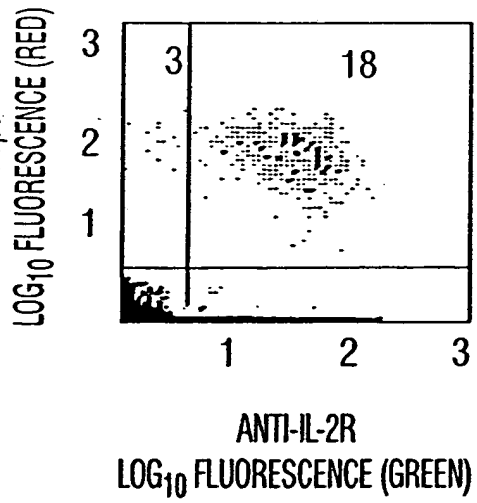


FIG. 8D

FIG.10A-1

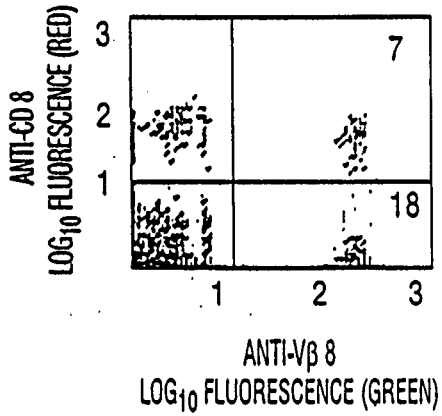


FIG. 10A-2

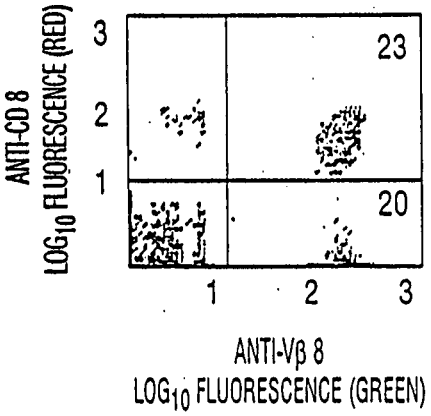


FIG. 10A-3

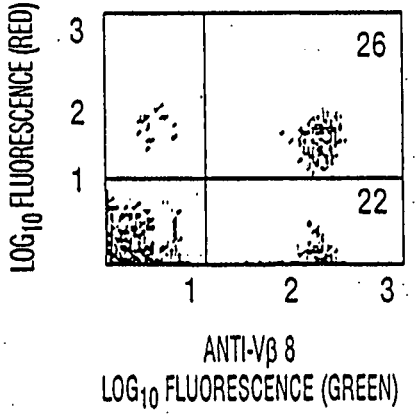


FIG. 10B-1

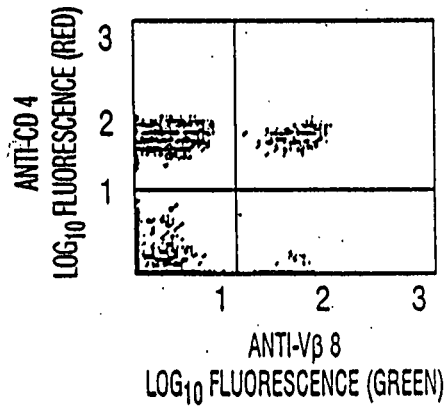


FIG. 10B-2

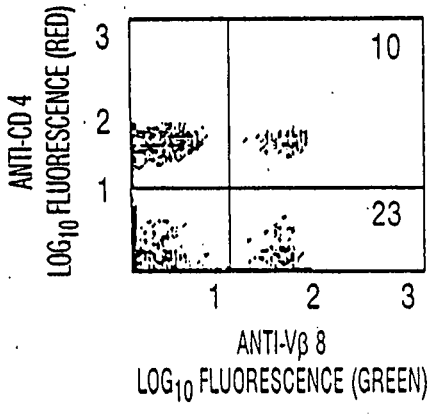
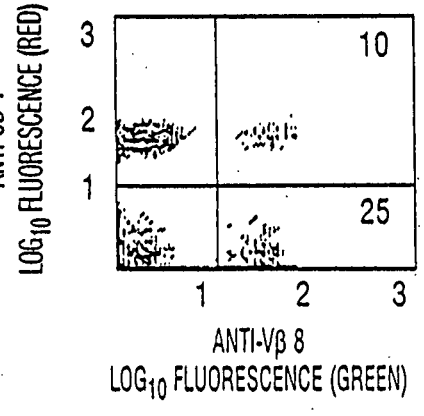


FIG. 10B-3



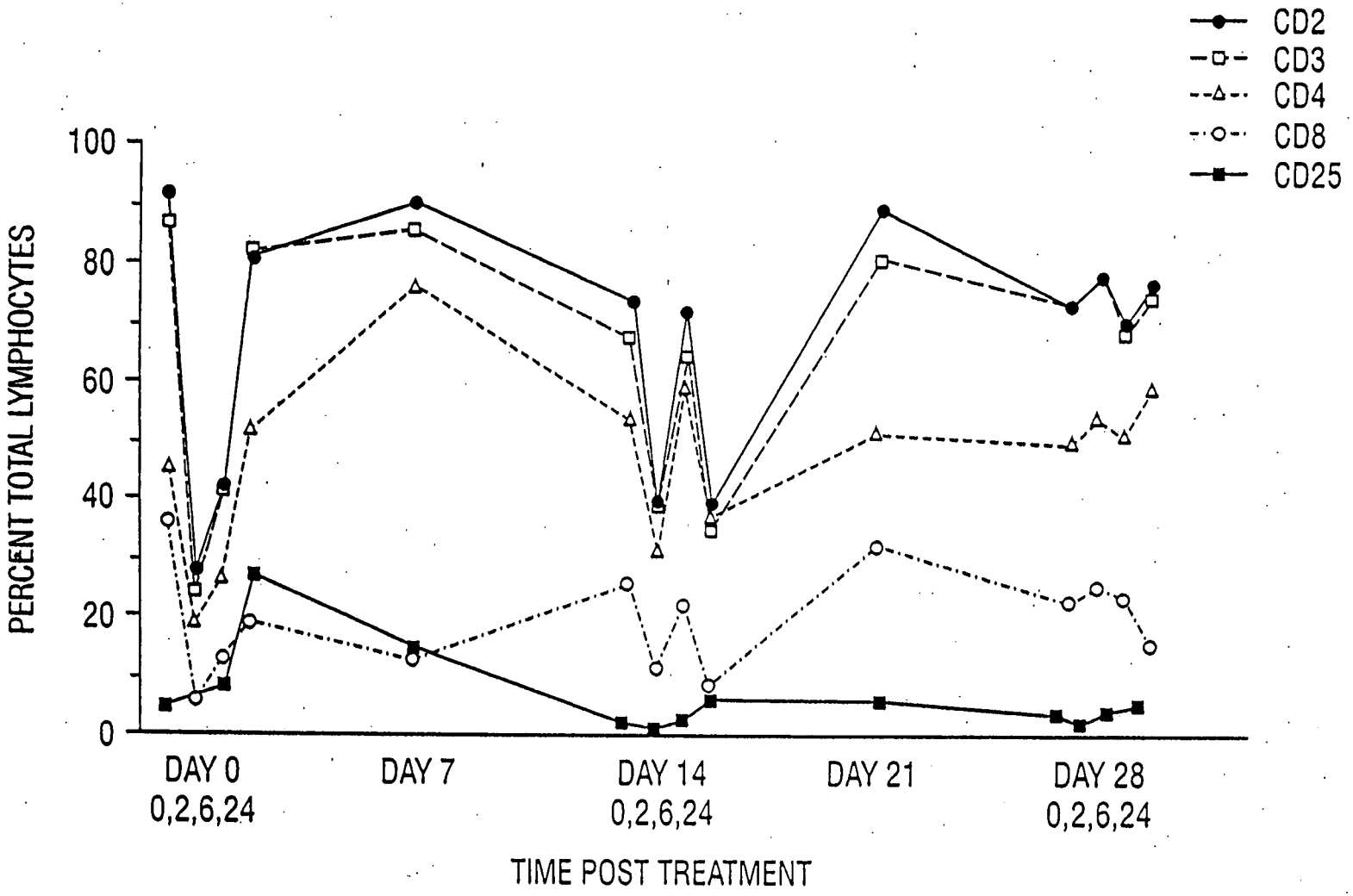

CD2
CD3
CD4
CD8
CD25
100
80
60
40
20
0
PERCENT TOTAL LYMPHOCYTES
DAY 0
0,2,6,24
DAY 7
DAY 14
0,2,6,24
DAY 21
DAY 28
0,2,6,24
TIME POST TREATMENT

FIG. 11

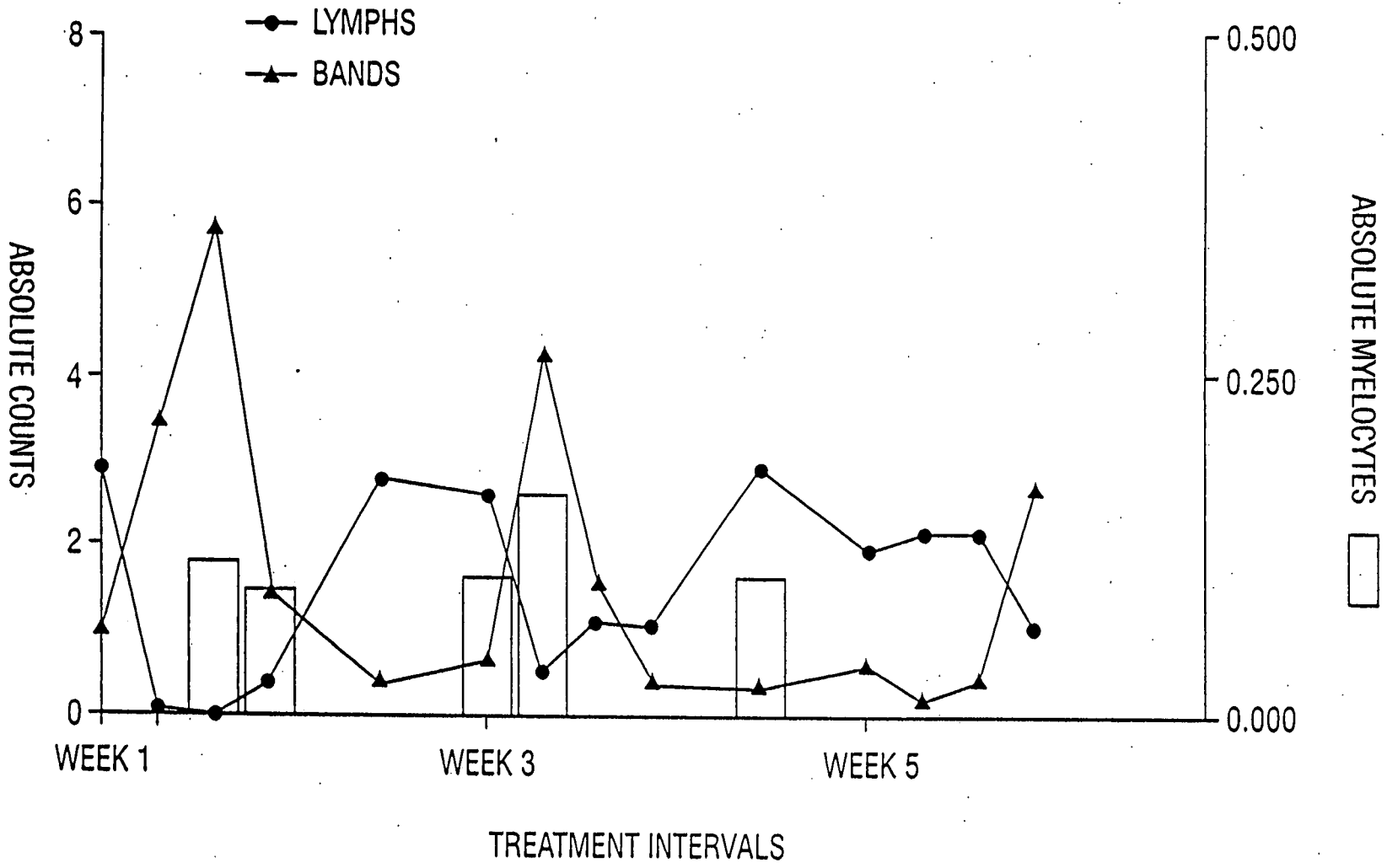


FIG. 12

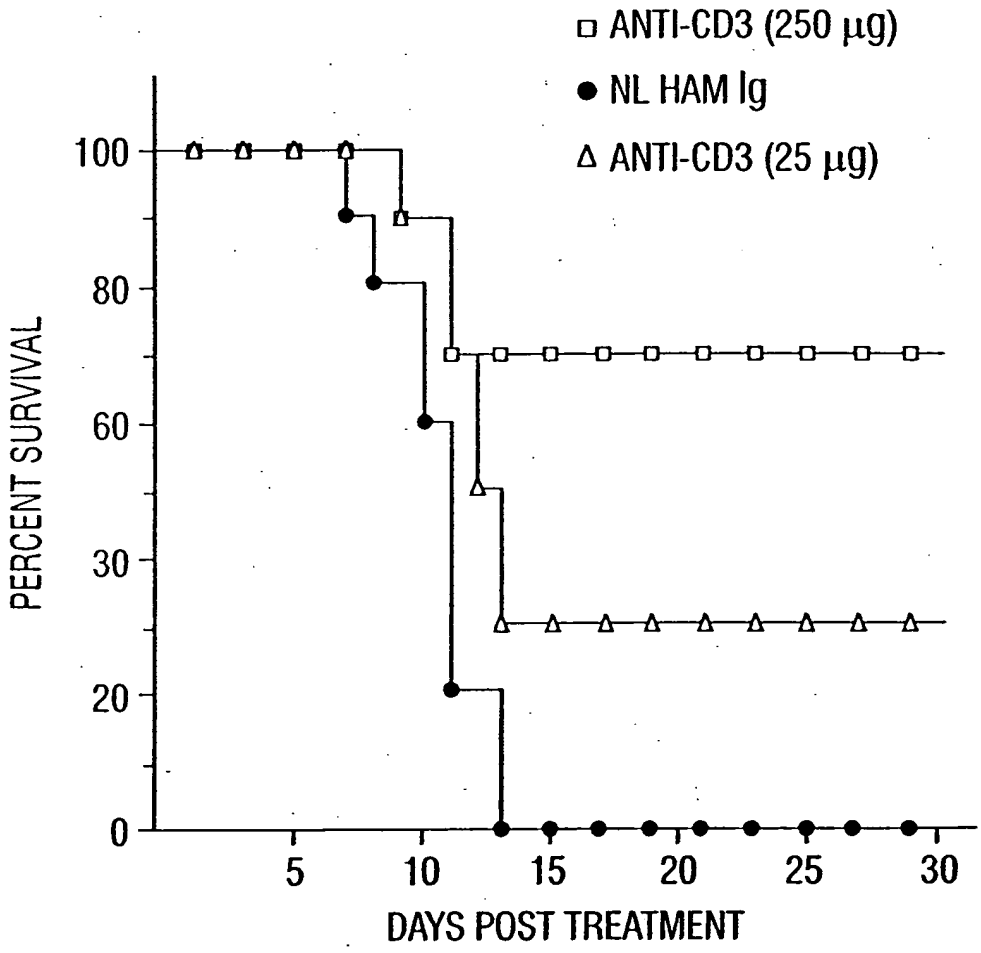

ANTI-CD3 (250 µg)
NL HAM Ig
ANTI-CD3 (25 µg)
PERCENT SURVIVAL
100
80
60
30
20
0
5
10
15
20
25
30
DAYS POST TREATMENT

FIG. 13

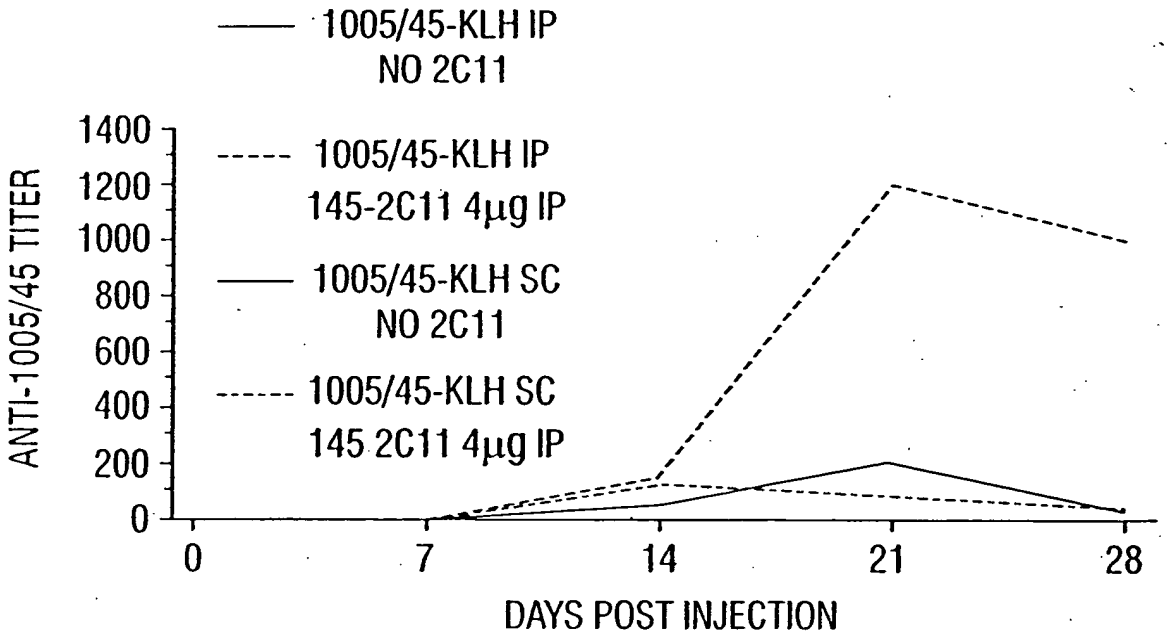

1005/45-KLH IP
NO 2C11
1005/45-KLH IP
145-2C11 4µg IP
1005/45-KLH SC
NO 2C11
1005/45-KLH SC
145 2C11 4µg IP
ANTI-1005/45 TITER
1400
1200
1000
800
600
400
200
0
0
7
14
21
28
DAYS POST INJECTION

FIG. 14

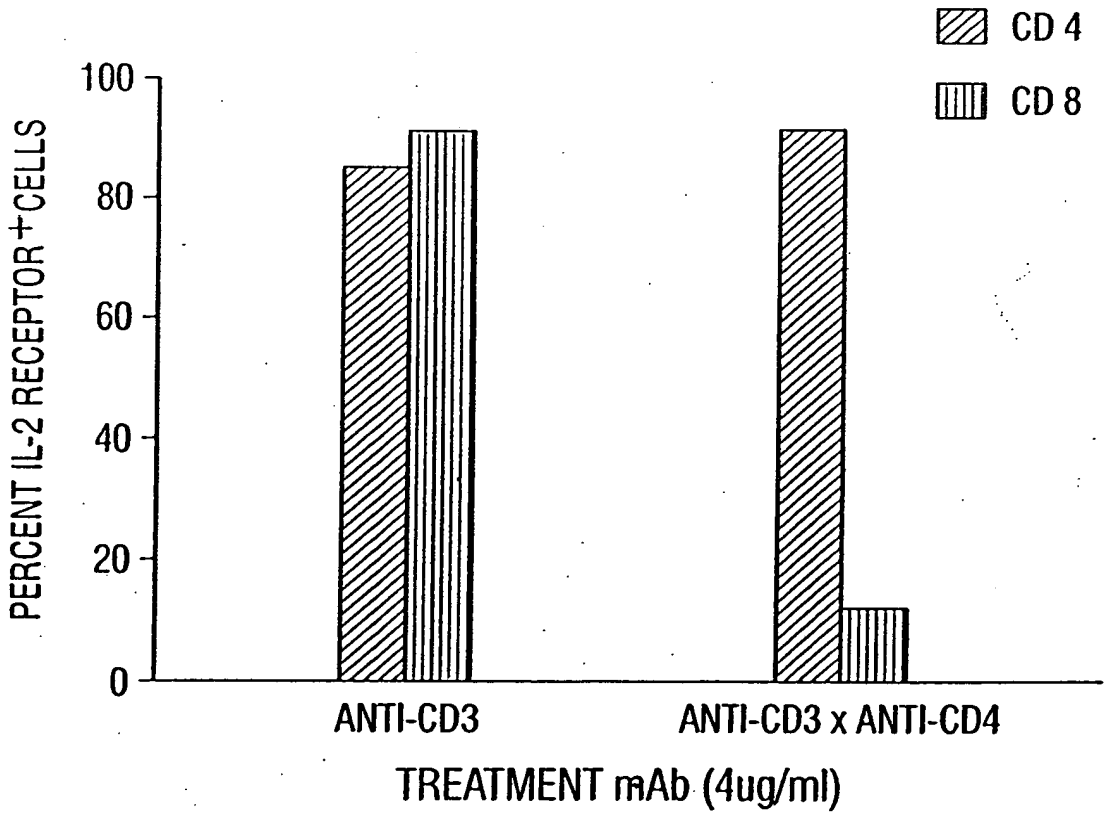

CD 4
CD 8
PERCENT IL-2 RECEPTOR+CELLS
100
80
60
40
20
0
ANTI-CD3
ANTI-CD3 x ANTI-CD4
TREATMENT mAb (4ug/ml)

FIG. 15

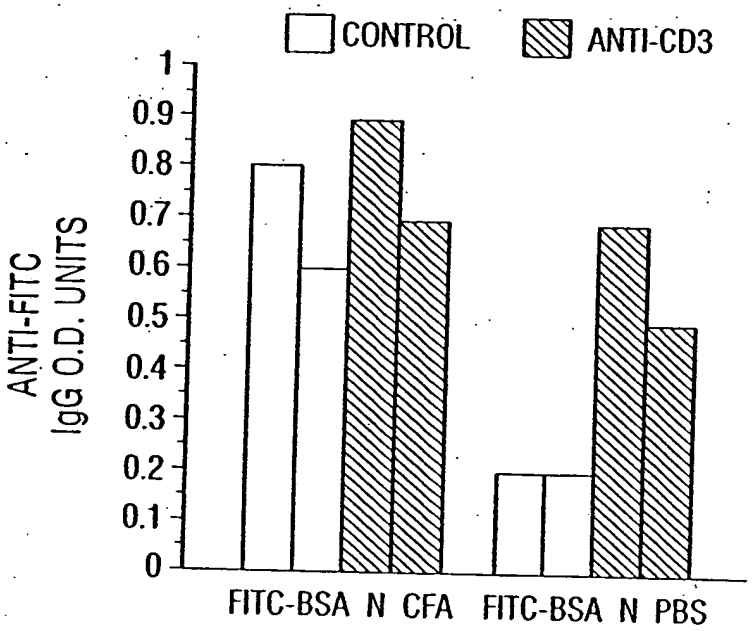


FIG. 16A

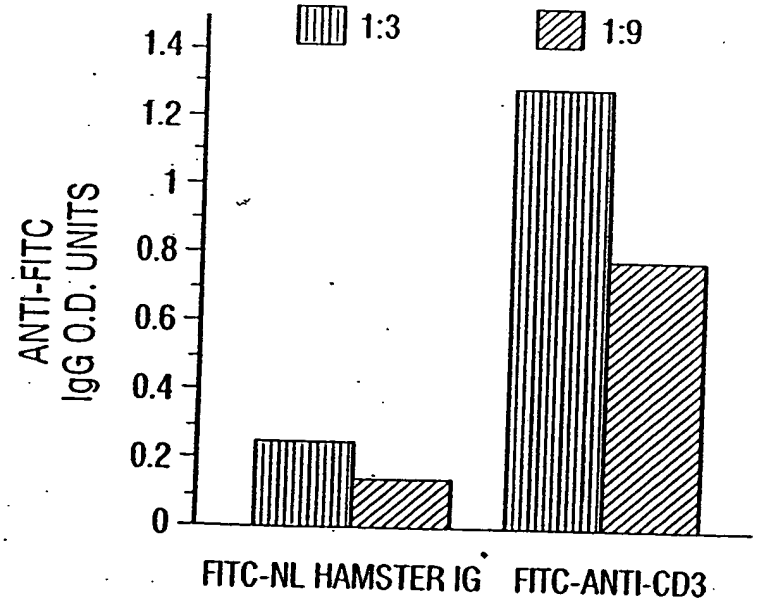


FIG. 16B

FIG. 17